

# Severe Acute Respiratory Syndrome (SARS): A Systematic Review

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## Abstract

Severe Acute Respiratory Syndrome (SARS) outbreak between 2002 to 2003 has accounted for the world panic. SARS was caused by a novel coronavirus (SARS-CoV) and had continued to expand into the 21<sup>st</sup> century (Tsang et al., 2003). Initially, the disease was observed to be incepted in a small district named as Shunde, which was present in the city named the Foshan City of Guangdong Province. From this area, it rapidly disseminated to Hong Kong and following it to the rest of North America, Asia, as well as Europe in the few months. The disease affected about 8437 patients, accounting for a mortality rate of 9.6 percent. World Health Organization (WHO), in May of the year 2005, forwarded a declaration that SARS disease has been eliminated, which ranked it as the second disease in humans to be labeled such following the first disease, i.e., smallpox. The civet cats isolated coronaviruses in China has substantial sequence homology with SARS-CoV, which indicates a zoonotic origin. Thereby this research paper reviews the general causes of SARS, its clinical manifestation, along with its treatment and prevention.

**Keywords:** SARS; Systematic; Review.

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## 1. Introduction

SARS (Severe Acute Respiratory Syndrome) is a disease of respiratory virus belonging to the zoonotic origin, which is caused by coronavirus of SARS. During November 2002 till July 2003, an upsurge in South China of SARS was the reason behind the ultimate 8,098 cases, which results in the death of 774 people in 37 countries, with most of the cases in China (i.e., 9.6% rate of a fatality) as per the reports of WHO. There were no patients reported of SARS since the year 2004. In the last months of 2017, the scientists in China followed the signs of the viruses by the intermediary civets to cave-dwelling bats in the Province of Yunnan in China.

SARS was a considerably unusual disease; by the end of the epidemic in the month of June 2003, there were 8422 patients reported with the fatality rate of 11 percent. The range of the case-fatality rate is from 0 percent to 50 percent, which depends on the age group of the infected patient. The patients having the age below 24 has the minimum potential to die, yet those having more than 65 are the most possibility to die. The basic path for the transfer of SARS is the link of the mucous membranes through the respiratory droplets or the fomites. While diarrhea is usual among the patients of SARS, the route of the fecal-oral is not found to be the usual path for the transfer.

The main number of reproduction of SARS,  $R_0$ , has a scale between 2 to 4, which is based on the various assessments. Control steps were announced in the month of April 2003, and this declined the rate to 0.4. The starting signs are similar to flu and can involve muscle pain, fever, cough, throat sore, lethargy signs, and the other non-particular signs. The single sign usual in all of the cases was found to be the fever more than 38°C (100 °F). SARS ultimately directs towards the breath shortening and pneumonia, either the active pneumonia through the virus of bacterial pneumonia.

The aggregate of the incubation duration for SARS is in between 4 to 6 days, though hardly it can be as short as a single day or as long as 2 weeks.

### 1.1. Problem Statement

WHO (The World Health Organization) announced extreme acute respiratory syndrome, which contained in the year 2003 on 9<sup>th</sup> July. During these years, four patients of SARS have been registered in China between December 2003 till January 2004. There are three special laboratories' incidents, which were the reason behind the infection. In a case among these, a sick lab work spread the virus to the other workers. The research of SARS specimens needs the BSL-3 service; some of the researches of the indirect SARS specimens may be performed at BSL-2 services.

The purpose of this research is to get an in-depth knowledge of SARS. It also has an objective to observe the reasons and the precautions of this disorder. Thus, below are the queries inspected throughout the research,

1. What are the basic reasons behind SARS?
2. What are the ways for the precautions for SARS?
3. What is the therapy of SARS?

## **2. Research Method**

There is a number of techniques that can be utilized to gather the data, and these techniques are accessible by the researchers, yet, the selection must be suitable and made after the analytical assessment of the targets. Therefore, the segment of the paper describes the techniques which are being utilized for the research and the representation of the evaluation segment. This segment is classified into the subheadings for the exact knowledge of technique, and the justification for the selection.

### **2.1 Research Context**

A lot of methodologies can be utilized by the researchers, yet the subject of the research must highlight the reasoning, in line with the subject. The subject of the research in this study depends on the descriptions, which are linked with SARS. The reasons are majorly linked with the description and the assessment of the disease. The subject of the research focuses on the reasons behind the SARS, precautions, and therapy. The main aim is to explain the SARS in details .

### **2.2 Research Philosophy**

A number of research ideologies are available for the researchers, such as;

1. Ontology,
2. Epistemology
3. Interpretivism
4. Positivism
5. Axiology
6. Realism

This study utilizes the realist approach for the interrogation as it was most suitable in terms of representing the syndrome. The realist approach is the most suitable for the assessment of the reasons through the observation of the qualitative statements. It is now easier than ever for the researchers to enhance the awareness of this syndrome by this structure. The realist approach is classified into two distinguished kinds, which are direct realism and the analytical realism techniques, yet, it is essential that every approach must be utilized by the researchers for the understanding of the connections between the independent and the dependent variables.

### **2.3 Measures**

The steps which are required to be taken by the researchers should be in line with the outcomes required to be attained. These steps must be taken after the proper consideration of the targets, or else, the dependency or the accuracy of the outcomes will be decreased.

For the finding of the outcomes of the research, the articles which are only 10 to 15 years old will be utilized. This will help to collect the data through the provision of the recent trends which are assessed in the syndrome. Moreover, it will offer an in-depth knowledge of the disease. Another significant step for this research is the choice of the articles through the use of the website such as Google Scholar. The study article has an objective to highlight the major reason behind the syndrome, as it is significant to utilize only the study articles of SARS.

### **2.4 Procedures**

This research selects a suitable process for the collection of data and the assessment to evaluate the SARS with the proper instructions and the realist approach. Firstly, the research questions are being determined, as it is one of the most significant parts of the collection of the data. Secondly, it has been examined that the questions are in line with the aims and targets of the study. The objectives and the questions of the research were described and represented by the writers to assess whether they are suitable or not. This will help to understand that if the targets and purpose of the study are accurate and can be relied upon or not.

Once the study articles and the queries are being gathered, the assessment process is easier. Then the research articles are being gathered to conduct the desk review. Yet, before conducting the process of desk review, it has been confirmed that every article was in accordance with the subject. Once the statements are extracted from these research articles and are compared, which is a very hard step and needed that the flow must not be affected during the assessment of the data. After the analytical review of the reasons, it has been made sure that the reasons and the flow under all of the headings are in accordance with the need and the meet the compliance along with the research queries.

After the analysis of the outcomes, the finalization has been performed by the researchers. Arguments for the writing of the descriptions and the final section is to provide the readers with a summarized form of the findings of the research. Thus, after the final section, it has been described in-depth, if it has everything linked with the research queries. With the help of the research queries, it is now easier to collect, analyze and complete all of the sections of this research; it is discussed again in-depth to increase the accuracy and the dependency of

the outcomes.

## 2.5 Data Collection Method

The research has utilized the qualitative approach to collect the data and the assessment as well. To collect the qualitative data, there a number of approaches that can be accessed by the researchers, for example, the questionnaires, the interviews, observations, and case studies. Yet, this study has utilized the qualitative approach to fulfill the needs of the research. The quantitative methodology is not appropriate for this research at the moment.

## 2.6 Data Analysis Method

There are different kinds of approaches available for the assessment of data and it has become essential that all of them must be assessed after the observation of the needs of the research for the enhancement of dependency and the accuracy. The approaches of the data analysis are mainly available in different kinds yet have classified into the quantitative and the qualitative patterns, yet, selection of the best is essential. The approach opted for the assessment is the desktop review approach, as this is the most appropriate method for the research. With the help of the various methods for the research analysis, it is now easier to assess this disease, regarding etiology, therapy as well as precautions. The researchers opted for the website of Google Scholar as it is found to be the most reliable website for the selection of the article, its evaluation as well as to compare the different articles. Additionally, the research article presented in the last 15 years is being considered for the review purpose. The review of all of the articles was performed analytically as it assisted in the analysis of the SARS in a complete possibility.

## 2.7 Sample Size, Sampling Method and Population

The size of the sample, approach and the population of the research is considered as the most significant framework for the observation of the analytical reviews, the approaches of the sampling are there in the different kinds and classified into the methods of probability sampling and non-probability sampling. This research selects the method of non-probability sampling as it offers the evaluation of all of the research targets in depth. Non-probability sampling methods are available in the various formats, yet, the style which has been selected in this research is purposive sampling method since it will offer the evaluation of the outcomes through the observation of the outcomes which depends on a specific purpose.

This sampling technique is used as it is offered in the selection of the research article dependent on the subject of the research. Additionally, the sample of the articles of the research was more than 20 articles for the analytical overview. This method of sampling helped in the selection of the most considerate articles linked with the subject. It also helped to understand the part of various researchers, and the arguments they include themselves to understand the syndrome.

## 3 SARS in a Whole Prospective

This part of the study will be discussed the followings:

1. Main Causes, Clinical Elements, Prevalence & Control.
2. Diagnosis
3. Precautions or the Preventions
4. Therapy or Treatment
5. Prognosis
6. Epidemiology

### 3.1 Main Causes, Clinical Elements, Prevalence & Control.

According to the study of Channappanavar et al. (2016), SARS causes due to the member mainly from a carnivorous family which can cause the common cold. From the research study, it has determined that in the year 2003, this epidemic started by causing the virus among mammals in the Chinese economy or state. It was the time when mammals started with a cough and sneeze due to SARS and as results, droplets due to sneezing started to expand to cause further virus among people of the state. People with SARS, when coughing or sneezes the droplets in saliva are infectious and these droplets spray itself in the air. Thereby, another person or individual catches SARS. If an individual with SARS, breaths or touches to the other individuals, it spreads the virus to other surfaces in the form of droplets. SARS virus found on the hands including tissues and various other surfaces and a virus remains for several times in the form of droplets on hands and tissues of an individual. This virus stays for more months or even for long days when the temperature becomes below freezing.

In addition to this, droplets go from one person to another in the form of close contact with each other as it had determined from various earlier cases of SARS (Channappanavar et al., 2016). In some cases, airborne transmission is a real possibility. The virus according to several research studies, also found in the stool of

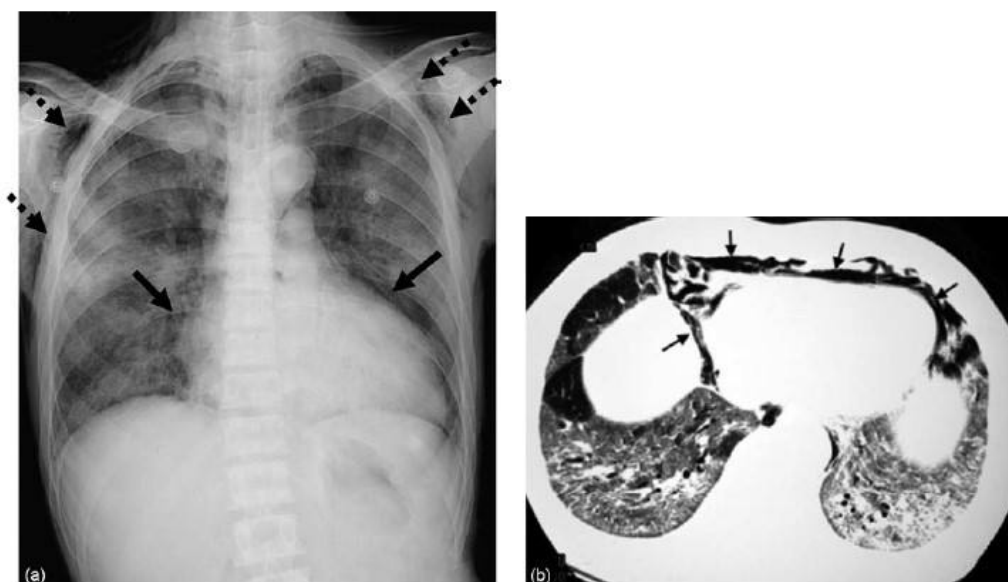
various persons and it stays long for even 3 or more than three days. Symptoms of SARS remain 2 to 10 days after when any person contacts with SARS virus from any place or another individual. People have determined with active symptoms of having SARS such as illness and a person remains contagious after the symptoms appear.

The study of de Wit et al. (2016), had defined SARS as the severe acute respiratory syndrome that was first established or discovered in Asia during the year-February 2003. This major outbreak lasted around for six months to spread the diseases and then it expanded in numerous countries including; South and North America, Europe etc. The study of de Wit et al. (2016), had defined the guidelines published by the Centers for Disease Control and Prevention (CDC), as according to the guidelines of Centers for Disease Control and Prevention (CDC), lab test is crucial to detect SARS virus because it includes in the blood of an individual or urine, stool tests are also necessary to determine the presence of SARS. According to the study of Channappanavar et al. (2016), there is no proper control to SARS virus but from the research, it has analyzed that various vaccines are behaving as the cure to prevent further risk of SARS. People with SARS should be admitted to hospitals immediately under the closest observation and supportive treatment is necessary which also includes; ventilator to provide oxygen to an individual.

The study of Menachery et al. (2016), had defined that several complications occur when a person is diagnosed with SARS. These complications include; having pneumonia, breathing problem due to which person needs oxygen or ventilator. In addition to this, illness due to SARS is fatal in some major cases significantly due to respiratory failure. Other complications due to SARS include heart and liver failure. People who are of 60 or more than 60 age, particularly those people who have diabetes and hepatitis are at the highest risk of vulnerable complexities or complications due to SARS (de Wit et al., 2016; Yang et al., 2017).

### 3.2 Diagnosis

The recent WHO identification of SARS needs the description of the clinical characteristics (fever  $\geq 38$  C, symptoms of respiration, radiographic pneumonia, and autopsy outcomes of persistent pathology in otherwise undefines illness) and in the existence of the virological evidence of SARS-CoV infection (which is positive RT-PCR for the existence of SARS-CoV RNA, seroconversion with particular antibody emerged in paired sera or virus isolation). In a practical manner, the prerequisite for the detection of SARS involve the existence of an epidemiological connection, instantly growing pneumonia repellent to standard therapy, clinical characteristics, and virological proof of SARS-CoV infection. An epidemiological connection, described as a background of contact with a SARS patient or visiting a hospital with nosocomial SARS outbreak, in the 10 days preceding disease onset, is helpful for the infected patients in regions of upsurge. Virtually all of the patients decline irrespective of the potent antibiotic therapy (Tsang et al., 2003), and main have lymphopenia and emerging transaminase standards.



**Figure 2** Radiography of a 52-year-old man on 12 days after onset of severe acute respiratory syndrome showing (a) chest X-ray features of pneumo-mediastinum (solid arrows) and surgical emphysema (dotted arrows), and (b) computed tomography features of pneumo-mediastinum (arrows) and bilateral ground-glass opacities.



A chest X-ray representing enhanced opacity in both lungs, detecting the pneumonia, in a SARS patient. SARS can be doubtful in a patient having:

- Any of the signs, which includes 38 °C (100 °F) or more fever, and
- Have a background of:
  1. Link (sexual or casual) with anyone who has diagnosed SARS in the last 10 days *or*
  2. Visit any of the areas highlighted by the World Health Organization (WHO) as the region with current domestic transfer of SARS.

For a situation to be found as a possibility, an X-ray of chest should be positive for atypical pneumonia or respiratory distress syndrome.

It has been defined by WHO that the class of "laboratory confirmed SARS" for the possible patients yet do not have a positive chest X-ray changes, but they have been tested positive for SARS depending on one of the acknowledged tests (ELISA, immunofluorescence or PCR).

The emergence of SARS in chest X-rays is not the same yet normally emerge as an abnormal patch of infiltrates.

### 3.3 Prevention

SARS has no vaccine. Quarantine and isolation are the basic successful methods effective for the prevention of the growth of SARS. Other steps for the prevention include:

- To wash hand
- To disinfect the areas for fomites
- Wear a mask of surgical
- Avoid the bodily fluids' contact
- Wash the private material of SARS patient in hot, soapy water (which includes utensils and dishes for eating, bedding, etc.)
- Keep children with signs home from school
- Usual hygiene steps
- Isolate oneself to the maximum for the reduction of chances of transfer of virus

### 3.4 Treatment

The therapy for SARS, managed during the catastrophic conditions of 2003, were highly unsystematic and was not backed up by the monitored trial information.

#### 3.4.1 Pharmacotherapy of SARS

Conceptually, there will be no indication of SARS if the effective antivirus agents are given to the disorder onset. Yet, the agents with proven effectiveness cannot be accessed despite the productive recommendations. Other than managerial treatment of the empirical antibiotics for the extreme community gained pneumonia, it is suggested to monitor the clinics to assess the effectiveness of the possible immunomodulating and antivirus agents. The clinical sufferings can be accessed by some agents utilized in 2003 upsurge, which are named as corticosteroids, convalescence serum, interferons, ritonavir/lopinavir, ribavirin, and immunoglobulin. In the past years, and before WHO described SARS, the infected individuals were being healed and cured with the wide-spectrum agent of antivirus, which named as corticosteroid and ribavirin. Almost 60 percent of hemoglobin of the patients declined by 2 g/dl after the therapy with ribavirin (1.2 g tid) for 14 days, and a greater amount of the dose was linked with the increased range of liver transaminase and bradycardia (Booth et al., 2003). The instant



cure of some of the first patients in Hong Kong has given a direction to adopt the mentioned as the benchmark antiSARS regimen in the year 2003 in Hong Kong and the other countries as well. Ribavirin is now found to be failed. The effectiveness of the other potential agents of anti-SARS-CoV for example antiproteases such as Kaletra (lopinavir 100 mg and ritonavir 400 mg for two weeks), with the integration of ribavirin as the starting therapy, was linked with the decline of mortality rate (2.3 percent versus 15.6 percent) and in the rate of intubation from 0 percent versus 11 percent when they are being contrasted with the past monitoring (Chu et al., 2004). Thus it has been observed that lopinavir/ ritonavir can be used for the starting therapy of the patients infected with SARS, preferably in an arrangement which is monitored examination. Unfavorable responses are frequent and involve extreme diarrhea, abdominal pain, headache, skin rash, insomnia, nausea, asthenia, and pancreatitis.

Interferon  $\alpha$ -n3,  $\alpha$ -n1, and b-1b and the human leukocyte interferon show overall cytopathic impacts of SARS-CoV in vitro. Patients of SARS who are cured with interferon alfacon-1 and corticosteroids have a lower rate for admission to ICU, mechanical ventilation, and death (Loutfy et al., 2003). SARS-CoV is a wrapped RNA virus that contains various structured proteins. Recently, various doses, for example, the total killed dose, a vaccine for the adenovirus vector, and the protein dose with the recombinant spike are being examined among the animals in the labs, but these are not prepared for the large clinical examinations.

#### **3.4.2 Immunomodulating Agents**

Management of corticosteroids for the deterioration of the SARS patients is linked with importance, and some of the times, drastic clinical and radiographic healings (Figure 1). Rather than skepticism, the immunomodulating drugs can be used for the rescue treatments. Patients who are suffering from pulse steroid therapy (such as methylprednisolone 250 to 500 mg daily for 3 to 5 days) did not have greater cumulative steroid dose or negative impacts, yet had less need if the oxygen and improved result of radiography, than their matches counterparts (Ho et al., 2003). Though a retrospective assessment represented a greater 30-day mortality rate among the patients having pulse methylprednisolone, this can be due to the greater possibility of utilizing this treatment in many extreme SARS patients. Corticosteroids are successful agents of anti-inflammatory, which remarkably decrease the rates of IFN- $\gamma$  inducible protein-10, monocyte chemoattractant protein-1 and interleukin-8 in SARS (Wong et al., 2004). The usage of higher doses of steroids was linked with sepsis, specifically ventilator-connected pneumonia, and even the structured infection of fungus. Almost 15 percent of the patients of SARS had MRI-proven avascular necrosis (AVN) of knees and hips (Griffith et al., 2005).

#### **3.4.3 Miscellaneous Agents**

Convalescence serum was managed to 19 patients of SARS in Hong Kong in the year 2003, and receivers had a smaller stay in the hospitals and lesser rate mortality than their matches (Soo et al., 2004). The potential transfer of SARS-CoV (and other pathogens), conceptual drawbacks of its pro-inflammatory activities, and the recent lack make this way of the possible treatment disagreeable. Several other agents are being recommended to be possibly effective for SARS, by the benefit of their in vitro or only in conceptual actions contrary to SARS-CoV. These involve synthetic RNA duplexes, glycyrrhizin (licorice extract) which targets both SARS-CoV genomes, heparin and antiplatelet agents, nelfinavir, niclosamide, rhinovirus 3C proteinase inhibitors, anti-tumor necrosis factor- $\alpha$ , aminopeptidase N inhibitor, sodium nitroprusside, and a monoclonal antibody against S1 protein (Tsang et al., 2004).

#### **3.4.4 Noninvasive Positive Pressure Ventilation (NIPPV)**

Almost 20 percent of the patients of SARS grown the syndrome of acute respiratory distress, which needs invasive mechanical ventilation linked with the nosocomial growth of SARS. Yet, NIPPV utilization among the SARS cases in Hong Kong was observed to be successful for the prevention of intubation and oxygenation, with no proof of nosocomial growth of SARS (Cheung et al., 2004).

Antibiotics have been failed since SARS is a viral disease. The cure of SARS is majorly helpful with the antipyretics, mechanical ventilation, and the supplementary oxygen as per the requirements. The medicines for the antiviral are being utilized along with the higher dosage of steroids to decrease the swelling of the lungs. SARS patients should be isolated, in the rooms having negative pressure, with the total precautions of nursing taken for the essential connection with the patients, for the limitation of the possibilities of medical individuals to get infected with SARS. As in the year 2017, there is no therapy or the protective dose for SARS, which has been presented to both secure and successful among humans. The discovery and the growth of the new doses and the drugs to cure SARS is a preference of the government and the bodies of public health all over the globe. MassBiologics, which is an NPO (a non-profit organization) involved to identify, grow and produce the organic treatments, is integrating with scientists at NIH and the CDC to develop a monoclonal antibody treatment, which defines the effectiveness in the models of animals.

### **3.5 Prognosis**

The aggregate time for the stay in hospital was 21 days for the majority of the patients in the year 2003 in Hong Kong, and the 21-day mortality rate ranges from 3.6 to 10 percent. The last patient fatality ratio for Hong Kong,

as well as Canada, was found to be 17 percent, because of greater mortality among the patients having bad prognoses. Bad prognostic characteristics anticipation of death or admission in ICU involved higher age, diabetes mellitus or other comorbid conditions, chronic hepatitis B cured with lamivudine, high serum lactate dehydrogenase, and high rate of neutrophil, and low rate of CD4 and CD8 lymphocyte.

Various finalized reports in China regarding the patients who recovered from SARS showed extreme long term sequelae. The typical basic disorders are osteoporosis, femoral necrosis, and pulmonary fibrosis, which have given a direction towards overall loss of working capability or capability of self-care.

### 3.6 epidemiology and Infection Control

SARS was a considerably unusual disease; by the end of the epidemic in June of the year 2003, the accident was 8422 patients having the rate of case-fatality of 11 percent.

The range of the case-fatality ratio is from 0 percent to 50 percent based on the age of the patient. Patients have age less than 24 years had the least possibility to die, and the patients have age more than 65 years and older had the most possibility to die.

The most significant standard for SARS is to make sure no more upsurge in the hospitals as well as society. Isolated nursing can be obtained in either the single rooms or even in the open wards, as long as they are completely managed and monitored. The rate of air exchange of 12 times per hour and a temperature of 20 C is found to be the requirement since the wearing of personal protective equipment (PPE) by the workers can be hot. Personal protective equipment must be offered to the trained workers involving the usage of gowns covering full-body and particular masks (for example, N95 masks). All of the workers are needed to obey rigid and systematic 'gowning' and 'degowning' processes. Precise individual cleanliness is needed. Diluted bleach is being utilized to clean all surfaces as well as the floor after an hour or after any possible impurity. As nebulizer treatment was supposed to be the reason for the most upsurge in the hospital of Hong Kong, this way of treatment is prohibited for patients with doubtful or possible SARS in Hong Kong.

### Conclusion

The study has defined the pharmacotherapy of severe acute respiratory syndrome (SARS), it has defined the cause, prevention, prevalence and control of severe acute respiratory syndrome. It has briefly defined the immunomodulating agents concerning SARS and the other miscellaneous agents. It had also explained the noninvasive pressure ventilation (Nippv). From the overall discussion, it concludes that the control on SARS might be possible but in some cases it causes vulnerable deaths and complications to individuals. Complications like heart and liver failure.

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